<Synthetic Organic Chemistry > Fine Organic Synthesis

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- Fine Organic Synthesis -

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Scope of Research

The research interests of the laboratory include the development of new synthetic methodology, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on "memory of chirality", nucleophilic catalysis for selective reactions, synthesis of unusual amino acids, visualization of molecular chirality by functionalized phenolphthalein, use of homooxacalixarene for molecular recognition, and the structural and functional investigation of heterochiral oligomers.

Research Activities (Year 2003)

Presentations

A Facile Asymmetric Synthesis of Tetrahydro-isoquinoline and Tryptoline Derivatives with a Quaternary Carbon Center at C(3), Ozturk O, Shimada S, Kawabata T, Fifth AFMC International Medicinal Chemistry Symposium, 14 October.

Memory of Chirality in Intramolecular Alkylation of Amino Acid Derivatives: A Facile Synthesis of Chiral Nitrogen-Containing Heterocycles, Kawabata T, Kawakami S, Majumdar S, Ozturk O, 15th International Symposium on Chirality, 22 October.

Effective Synthesis of Optically Active Naphthalene Oligomers, Tsubaki T, Miura M, Morikawa H, Tanaka H, Furuta T, Tanaka K, Kawabata T, Fuji K, 15th International Symposium on Chirality, 22 October.

New C_2-Symmetric PPY Analogues as Catalysts for Enantioselective Acylation, Schedel H, Kawabata T, The Nineth International Kyoto Conference on New Aspects of Organic Chemistry, 10 Novemmber.

Asymmetric Induction Based on Dynamic Chirality of Enolates, Kawabata, T, The 2nd Takeda Science Foundation Symposium on PharmaSciences, 2 December.

Grants

Kawabata T, Design of a New Generation of Nucleophilic Catalysts and Selective Reactions, Grant-in-Aid for Scientific Research (B) (2), 1 April 2002 - 31 March 2005.

Tsubaki K, Visualization of Molecular Information using Phenolphthalein Derivatives. Grant-in Aid for Scientific research (C) (2), 1 April 2002 - 31 March 2004.

Kawabata T, Majundar S, Asymmetric Cyclization based on the Dynamic Chirality of Enolates, Grant-in-Aid for Scientific Research, 31 October 2003 - 30 October 2005.

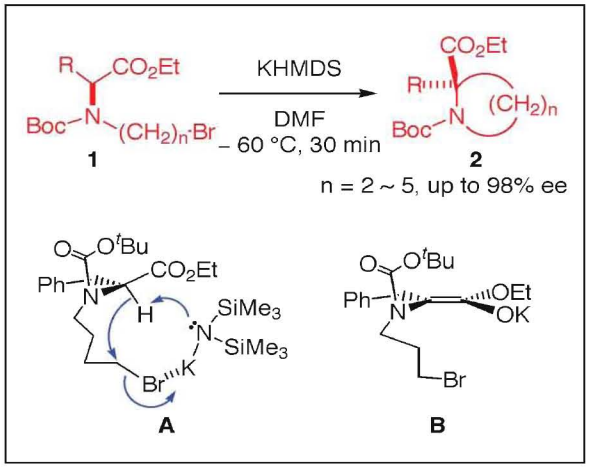
Kawabata T, Schedel H, Development of a New Generation of Chiral Nucleophilic Catalysts, Grant-in-Aid for Scientific Research, 3 June 2003 - 2 June 2005.

Award

MIURA M, Best Poster Award, Effective Synthesis of

New Protocol for Asymmetric Cyclization of Amino Acid Derivatives

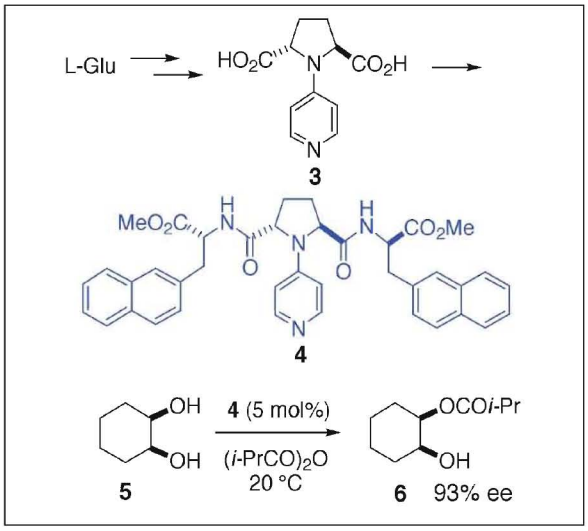
N-(ω-Bromoalkyl)-α-amino acid derivatives **1**, readily prepared from natural α-amino acids, gave cyclic amino acids with a quaternary stereocenter by treatment with KHMDS in DMF. Chirality of the parent amino acids was almost completely preserved during an enolate-formation and cyclization process, giving aza-cyclic amino acids in up to 98% ee in retention of configuration. This method is applicable to the asymmetric synthesis of azetidine (n=2), pyrrolidine, (n=3), piperidine (n=4), and azepane (n=5) derivatives. Mechanistic investigation indicated that the asymmetric cyclization proceeds via an axially chiral enolate intermediate (**B**), and not through a concerted S_Ei process (**A**).



Kawabata T, Kawakami S, Majumdar S, *J. Am. Chem. Soc.* **2003**, *125*, 13012-13013.

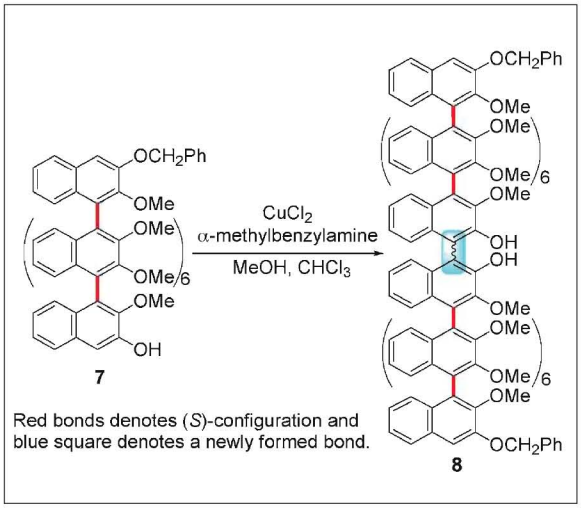
C_2-Symmetric PPY Analogues as Catalysts for Enantioselective Acylation

Combinatorial synthesis of C_2-symmetric pyrrolidinopyridine (PPY) analogues was accomplished by condensation of key intermediate **3**, obtained from L-glutamic acid, and variety of amino acid derivatives. A representative structure is shown as **4**. Catalyst **4** showed higher enantioselectivity than the corresponding mono-substituted PPY surrogate in asymmetric acylation of alcohols. Desymmetrization of meso-1,2-diol **5** with isobutyric anhydride in the presence of 5 mol% of **4** at room temperature gave **6** in in 75% yield and in 93% ee. Transition-state hydrogen bonding between substrate **5** and an acylpyridinium intermediate generated from **4** was suggested to be critical for the asymmetric induction.



Effective Synthesis of Optically Active Naphthalene Oligomers

The helical structure is one of the most ordered structures and packs molecular information into a restricted space. Rod-shaped oligo(2,3-dioxyfunctionalized) naphthalenes connected at their 1,4-positons are the molecules of interest because of their highly ordered helical structure. Highly diastetreoselective synthesis of them was accomplished by second order asymmetric transformation (i.e. epimerization of the axis together with diastereoselective crystallization). Oxidative coupling of octanaphthalene (*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*)-**7** in the presence of $CuCl_2$ and α-methylbenzylamine gave homochiral hexadecanaphthalene (*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*)-**8** in 70% yield together with (*S*,*S*,*S*,*S*,*S*,*S*,*S*,*R*,*S*,*S*,*S*,*S*,*S*,*S*,*S*,*S*)-isomer in 8% yield (79% de).



Tsubaki K, Miura M, Morikawa H, Tanaka T, Kawabata T, Furuta T, Tanaka K, Fuji K, *J. Am. Chem. Soc.*, **2003**, *125*, 16200-16201.

Chiral Oligo-Naphthalene Derivatives, 9th Summer Meeting on Functional Host-Guest Chemistry (Fukuoka), 21 Aug. 2003.